

(i) XY is excluded as group of formula -CH=CH- if R<sup>1</sup> is a hydrogen atom or a C<sub>1-4</sub>-alkyl group and R<sup>2</sup> is a monocyclic hetero aromatic having a N atom and/or a S atom in its ring and a C<sub>1</sub>-alkyl substituent and

(ii) XY is excluded as group of formula -CH<sub>2</sub>-CH-OP if R<sup>1</sup> is a hydrogen atom or a C<sub>1-4</sub>-alkyl group and R<sup>2</sup> is a monocyclic hetero aromatic having a N atom or a N atom and a S atom or a N atom and an O atom in its ring and a C<sub>1</sub>- alkyl substituent.

*E1  
CUT*  
23. (Amended) A compound according to claim 22, wherein the substituents of the monocyclic aromatic and/or hetero aromatic are a C<sub>1-6</sub>-alkyl, C<sub>2-6</sub>-alkenyl or C<sub>2-6</sub>-alkynyl group or a halogen atom.

24. (Amended) A compound according to claim 22, wherein the monocyclic aromatic and monocyclic hetero aromatic, respectively, is provided with 1, 2 or 3 substituents and the hetero aromatic is provided with 1, 2 or more hetero atoms.

*E8*  
Please add new claim 25:

*E9*  
25. (New) A compound according to claim 23, wherein the substituents of the monocyclic aromatic and/or hetero aromatic are C<sub>1-4</sub>-alkyl, C<sub>2-4</sub>-alkenyl and C<sub>2-4</sub>-alkynyl groups.

#### REMARKS

Claims 1-14, 18-20 and 22-25 will be pending in this application upon entry of the present amendment. Claims 1-5, 7-14 and 22-24 have been amended.

The claims have been amended to replace the phrase "Epothilone derivative" with "A compound." Support for this amendment is found in the Specification at page 5, lines 1-2, where disclosed formulas are described as "The compounds according to the invention."

Each occurrence of the term "alkinyl" has been replaced with the term "alkynyl" to correct typographical errors. Support in the Specification for this amendment can be found at page 4, lines 12, 19, 22 and 23.

The term “monocyclic” has been inserted before the terms “aromatic” and “heteroaromatic” in claims 8 and 24. Support for these amendments is found in the Specification at page 4, lines 7 and 16.

Claim 5 has been amended to include the recitation that “XY is excluded as group of formula -CH<sub>2</sub>-CH-OP if R<sup>1</sup> is a hydrogen atom or a C<sub>1-4</sub>-alkyl group and R<sup>2</sup> is a monocyclic hetero aromatic having a N atom or a N atom and a S atom or a N atom and a O atom in its ring and a C<sub>1</sub>-alkyl substituent.”

Claim 23 has been amended to delete the recitation of “C<sub>1-4</sub>-alkyl, C<sub>2-4</sub>-alkenyl and C<sub>2-4</sub>-alkinyl groups.” New claim 25 has been added to recite this class. Support for new claim 25 can be found in the Specification at page 6 (formula (6)) and page 4, lines 7-26. No new matter has been added.

Applicants gratefully acknowledge the Examiner’s indication that claims 1, 2, 9 and 10 are in condition for allowance. As discussed above, claims 1 and 2 have been amended to replace the phrase “Epothilone derivative” with “A compound.” Claims 9 and 10 have been amended to replace the language “of formula” with “of claim.” These amendments are merely stylistic in nature and do not add any new matter. Thus, claims 1, 2, 9 and 10 remain allowable.

## **I. Rejection Under 35 U.S.C. §112, Second Paragraph**

### **A. Each occurrence of “alkinyl” has been replaced with “alkynyl” in Claims 4, 7, 11, 12 and 23**

Claims 4, 7, 11, 12 and 23 stand rejected under 35 U.S.C. §112, second paragraph, for allegedly being indefinite due to the recitation of the term “alkinyl.” As suggested by the Examiner, Applicants have amended claims 4, 7, 11, 12 and 23 to replace each occurrence of “alkinyl” with “alkynyl.”

Accordingly, Applicants believe that the rejection of claims 4, 7, 11, 12 and 23 under 35 U.S.C. §112, second paragraph, for alleged indefiniteness has been overcome and should be withdrawn.

### **B. The term “monocyclic” has been inserted before aromatic and heteroaromatic in Claims 8 and 24**

Claims 8 and 24 stand rejected under 35 U.S.C. §112, second paragraph, for allegedly being indefinite due to the recitation of the terms aromatic and heteroaromatic without the being preceded by monocyclic as in claim 4 from which each depends. As suggested by the

Examiner, Applicants have amended claims 8 and 24 to insert the term “monocyclic” before aromatic and heteroaromatic.

Accordingly, Applicants believe that the rejection of claims 8 and 24 under 35 U.S.C. §112, second paragraph, for alleged indefiniteness has been overcome and should be withdrawn.

**C. Claim 14 is Not Indefinite**

Claim 14 stands rejected under 35 U.S.C. §112, second paragraph, for allegedly being indefinite due to R<sup>2</sup> representing a monocyclic aromatic ring or a monocyclic heteroaromatic ring when the claim comprises the steps of claims 9 or 10 wherein R<sup>2</sup> is either boron or a halogen. Applicants respectfully disagree.

Claims 9 and 10 relate to the preparation of intermediates which are useful in the synthesis of epothilone derivatives. These intermediates can then be used in the subsequent synthesis of epothilone derivatives such as those encompassed by claim 14. The boron or halogen functionality at this position allows for the synthesis of epothilone derivatives with different monocyclic aromatic or a monocyclic heteroaromatic rings at this position. Thus, the method of claim 14 can comprise a step of the method of claim 9 or claim 10.

Accordingly, Applicants believe that the rejection of claim 14 under 35 U.S.C. §112, second paragraph, for alleged indefiniteness has been overcome and should be withdrawn.

**D. Claim 23 Has Been Amended to Delete the Recitation of “C<sub>1-4</sub>-alkyl, C<sub>2-4</sub>-alkenyl and C<sub>2-4</sub>-alkinyl groups”**

Claim 23 stands rejected under 35 U.S.C. §112, second paragraph, for allegedly being indefinite due to the recitation of “C<sub>1-4</sub>-alkyl, C<sub>2-4</sub>-alkenyl and C<sub>2-4</sub>-alkinyl groups” and “fluoro, chloro, bromo or iodo.” Claim 23 has been amended to delete this recitation. New claim 25 relates to this subject matter and depends from claim 23.

Accordingly, Applicants believe that the rejection of claim 23 under 35 U.S.C. §112, second paragraph, for alleged indefiniteness has been overcome and should be withdrawn.

**II. Rejection Under 35 U.S.C. §102(e)**

Claims 3-8, 12-14, 18-20 and 22-24 have been rejected under 35 U.S.C. §102(e) for allegedly being anticipated by U.S. Patent No. 6,380,394 to Nicolaou (the “‘394 patent”).

In particular, the Examiner has pointed to compound nos. 7002, 7004, 7005, 7006 (the “compounds of FIG. 16”) and 8000 and 8001 (the “compounds of FIG. 19”). The compounds of FIG. 16 are macrolides wherein R<sup>2</sup> is halogen or a monocyclic hetero aromatic having a N atom in its ring. The compounds of FIG. 19 are those wherein R<sup>2</sup> is a halogen or a mono- or bi- cyclic hetero aromatic having a N atom or a N atom and a S atom or a N atom and a O atom in its ring. None of the compounds of FIGS. 16 or 19 possess hydroxy protecting groups.

Claim 3 relates to compounds wherein R<sup>2</sup> is halogen and XY is -CH<sub>2</sub>-CH-OP or -CH=CH-. None of the compounds of FIGS. 16 or 19 in the ‘394 patent are those wherein R<sup>2</sup> is halogen and XY is -CH<sub>2</sub>-CH-OP or -CH=CH-. Furthermore, there are no compounds disclosed in the ‘394 patent whererin R<sup>2</sup> is halogen and XY is -CH<sub>2</sub>-CH-OP or -CH=CH-. Thus, the compounds of the ‘394 patent do not anticipate claim 3.

Claim 4 relates to compounds wherein R<sup>2</sup> is an optionally substituted monocyclic aromatic, XY is -CH<sub>2</sub>-CH-OP or -CH=CH- and the remaining hydroxyl group is protected. None of the compounds of FIGS. 16 or 19 or any other compounds of the ‘394 patent which have the same macrolide core structure as the compounds of claim 4 possess protected hydroxyl groups. Thus, the compounds of ‘394 patent do not anticipate claim 4.

Claim 5 has been amended to include the recitation that “XY is excluded as group of formula -CH<sub>2</sub>-CH-OP if R<sup>1</sup> is a hydrogen atom or a C<sub>1-4</sub>-alkyl group and R<sup>2</sup> is a monocyclic hetero aromatic having a N atom or a N atom and a S atom or a N atom and a O atom in its ring and a C<sub>1</sub>-alkyl substituent.” Thus, the compounds of the ‘394 patent do not anticipate amended claim 5.

Claim 6 is a dependent claim relating to narrower embodiments of claims 1, 2, 3, 4, 5, or 22. In view of the allowance of claims 1 and 2, the amendment of claim 5 and the remarks in connection with claims 3, 4 and 22 (the rejection of claim 22 is addressed below), Applicants believe that the compounds of the ‘394 patent do not anticipate claim 6.

Claim 7 is a dependent claim relating to narrower embodiments of claims 4, 5, 6 or 22. In view of the amendment of claim 5 and the remarks in connection with claims 4, 6 and 22, Applicants believe that the compounds of the ‘394 patent do not anticipate claim 7.

Claim 8 is a dependent claim relating to narrower embodiments of claims 4, 5, 6, 7 or 22. In view of the amendment of claim 5 and the remarks in connection with claims 4, 6, 7 and 22, Applicants believe that the compounds of the ‘394 patent do not anticipate claim 8.

Claim 12 relates to a process for the preparation of a compound of claim 4 by subjecting a compound of claim 3 to a coupling reaction. As discussed above, the ‘394 patent

does not disclose any compounds with the core macrolide structure of the present claims wherein the hydroxy groups are protected. Accordingly, neither does the '394 patent disclose methods for the preparation of such compounds. Thus, the methods of the '394 patent do not anticipate claim 12.

Claim 13 relates to a process for the preparation of a compound of claim 5 comprising deprotecting a compound of claim 4. As discussed above, the '394 patent does not disclose any compounds with the core macrolide structure of the present claims wherein the hydroxy groups are protected. Accordingly, neither does the '394 patent disclose methods for the deprotection of such compounds. Thus, the methods of the '394 patent do not anticipate claim 13.

Claim 14 relates to a process for the preparation of a compound of claim 5 comprising the process steps of claims 9-13. As discussed above, the '394 patent does not disclose any compounds with the core macrolide structure of the present claims wherein the hydroxy groups are protected. Accordingly, neither does the '394 patent disclose methods for the deprotection of such compounds. Thus, the methods of the '394 patent do not anticipate claim 14.

Claims 18 and 19 relate to a pharmaceutical composition comprising a compound of claim 1-8 or 22 and optionally carriers, diluents and/or auxiliary agents. In view of the allowance of claims 1 and 2, the amendment of claim 5 and the remarks in connection with claims 3, 4, 6-8 and 22, Applicants believe that the compounds of the '394 patent do not anticipate claim 18 or 19.

Claim 20 relates to a method of protecting plants in agriculture and/or forest culture and/or horticulture, comprising administering a therapeutically effective amount of at least one compound of claim 1 and optionally carriers, diluents and/or auxiliary agents. As stated by the Examiner (Office Action, page 4, paragraph 7, line 3) the '394 patent discloses the use of compounds for preventing mitosis in cancer cells. Nowhere in the '394 patent is there disclosed a method for protecting plants comprising administering any compound, let alone a compound of the present claims. Thus, the disclosure of the '394 patent does not anticipate claim 20.

Amended claim 22 relates to compounds wherein  $R^2$  is an optionally substituted monocyclic aromatic, XY is  $-\text{CH}_2\text{-CH-OP}$  or  $-\text{CH=CH-}$ , and XY is excluded as group of formula  $-\text{CH}_2\text{-CH-OP}$  if  $R^1$  is a hydrogen atom or a  $C_{1-4}$ -alkyl group and  $R^2$  is a monocyclic hetero aromatic having a N atom or a N atom and a S atom or a N atom and a O atom in its ring and a  $C_{1-}$  alkyl substituent. All of the compounds of the '394 patent possessing a

monocyclic hetero aromatic group are those containing a N atom or a N atom and a S atom or a N atom and a O atom. Thus, the compounds of the '394 patent do not anticipate amended claim 22.

Claims 23 and 24 are dependent claims relating to narrower embodiments of claim 22. In view of the above remarks regarding claim 22, Applicants believe that the compounds of the '394 patent do not anticipate claim 23 or claim 24.

Accordingly, in view of the above amendments and remarks, Applicants believe that the rejection of claims 3-8, 12-14, 18-20 and 22-24 under 35 U.S.C. §102(e) have been overcome and must be withdrawn.

### **III. Rejection Under 35 U.S.C. §102(b)**

Claims 4, 5, 7, 8 and 22-24 have been rejected under 35 U.S.C. §102(b) for allegedly being anticipated by Nicolaou *et al.*, *Chem. -- Eur. J.* 3(12):1971-1986(1997) ("Nicolaou").

In particular, the Examiner has pointed to compound no. 30 on page 1973 of Nicolaou. Applicants respectfully point out that the stereochemistry of the epoxide ring of compound no. 30 is the reverse of that of the compounds of the present invention. Applicants believe that the Examiner intended to point to compound no. 2 on page 1973 and will address the 102(b) rejection in view of compound no. 2. Applicants respectfully request confirmation that the Examiner intended to point to compound no. 2 of Nicolaou.

Compound no. 2 of Nicolaou is a macrolide possessing an R<sup>2</sup> group corresponding to a monocyclic hetero aromatic group containing one N and one O atom.

Claim 4 relates to a macrolide compounds wherein both hydroxyl groups are protected. Neither compound no. 2 nor any other compounds of Nicolaou which have the same macrolide core structure as the a compound of claim 4 possess any hydroxyl protecting groups. Accordingly, the compounds of Nicolaou do not anticipate claim 4.

Claim 5 has been amended to include the recitation that "XY is excluded as group of formula -CH<sub>2</sub>-CH-OP if R<sup>1</sup> is a hydrogen atom or a C<sub>1-4</sub>-alkyl group and R<sup>2</sup> is a monocyclic hetero aromatic having a N atom or a N atom and a S atom or a N atom and an O atom in its ring and a C<sub>1</sub>-alkyl substituent." All of the compounds of Nicolaou are those wherein R<sup>2</sup> is a monocyclic hetero aromatic having a N and S atom or a N and O atom. Compound no. 2 of Nicolaou is that wherein R<sup>2</sup> is a monocyclic hetero aromatic having a N and O atom. Thus, the compounds of Nicolaou, including compound no. 2, do not anticipate amended claim 5.

Claim 7 is a dependent claim relating to narrower embodiments of claims 4, 5, 6 or 22. In view of the amendment of claim 5 and the remarks in connection with claims 4 and 22

(the rejection of claim 22 is addressed below), Applicants believe that the compounds of Nicolaou do not anticipate claim 7.

Claim 8 is a dependent claim relating to narrower embodiments of claims 4, 5, 6, 7 or 22. In view of the amendment of claim 5 and the remarks in connection with claims 4, 7 and 22, Applicants believe that the compounds of Nicolaou do not anticipate claim 8.

Amended claim 22 relates to compounds wherein R<sup>2</sup> is an optionally substituted monocyclic aromatic, XY is -CH<sub>2</sub>-CH-OP or -CH=CH-, and XY is excluded as group of formula -CH<sub>2</sub>-CH-OP if R<sup>1</sup> is a hydrogen atom or a C<sub>1-4</sub>-alkyl group and R<sup>2</sup> is a monocyclic hetero aromatic having a N atom or a N atom and a S atom or a N atom and an O atom in its ring and a C<sub>1</sub>- alkyl substituent. As discussed above, all of the compounds of Nicolaou are those wherein R<sup>2</sup> is a monocyclic hetero aromatic having a N and S atom or a N and O atom. Compound no. 2 of Nicolaou is that wherein R<sup>2</sup> is a monocyclic hetero aromatic having a N and O atom. Thus, the compounds of Nicolaou do not anticipate amended claim 22.

Claims 23 and 24 are dependent claims relating to narrower embodiments of claim 22. In view of the above remarks regarding claim 22, Applicants believe that the compounds of Nicolaou do not anticipate claim 23 or claim 24.

Accordingly, in view of the above amendments and remarks, Applicants believe that the rejection of claims 4, 5, 7, 8 and 22-24 under 35 U.S.C. §102(b) have been overcome and must be withdrawn.

### CONCLUSION

Applicants believe that the rejections have been successfully overcome and that the pending claims are in condition for allowance. Withdrawal of the Examiner's rejections and allowance of the application are respectfully requested. If the Examiner has any questions or suggestions to expedite allowance of this application, he is respectfully invited to call the undersigned to discuss the matter further.

Respectfully submitted,

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Date May 22, 2003

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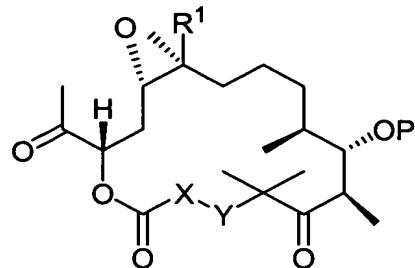
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Enclosures

**EXHIBIT A**

**MARKED-UP VERSION OF THE AMENDED CLAIMS**

1. (Amended) [Epothilone derivative] A compound of the formula [(2)]:



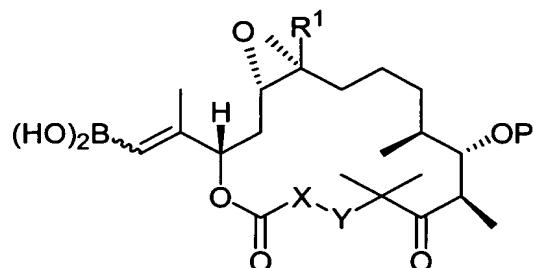
wherein

$R^1$  is a H atom or a  $C_1$ - to  $C_8$ -alkyl group,

$X-Y$  is a group of the formula  $-CH_2CH-OP$  or  $-CH=CH-$ , and

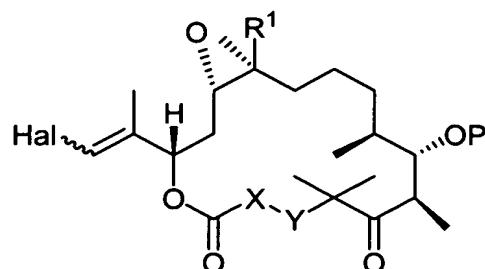
$P$  is a protecting group.

2. (Amended) [Epothilone derivative] A compound of the formula [(3)]:



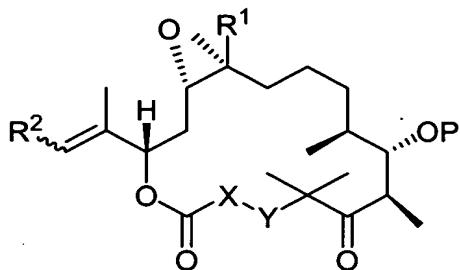
wherein the radicals are as defined in claim 1.

3. (Thrice Amended) [Epothilone derivative] A compound of formula [(4)]:



wherein the residues R<sup>1</sup>, X-Y and P are defined as in claim 1, and Hal is a halogen.

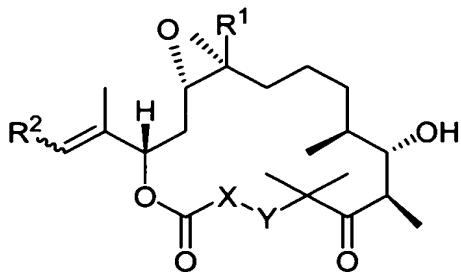
4. (Twice Amended) [Epothilone derivative] A compound of the formula [(5)]:



wherein the residue R<sup>1</sup> is a hydrogen atom or a C<sub>1-8</sub>-alkyl group, and P is a protective group and X-Y is a group of formula -CH<sub>2</sub>CH-OP or CH=CH, and R<sup>2</sup> is a monocyclic aromatic which can be substituted by a halogen atoms and/or OR<sup>4</sup>- and/or NR<sup>5</sup>R<sup>6</sup>- and/or alkyl, alkenyl and/or **[alkinyl]** **alkynyl** groups in ortho- and/or meta- and/or para-position, or a monocyclic 5- or 6-membered hetero aromatic, which can be provided with one or several O- and/or N- and/or S-atoms in the ring and/or which can be provided with OR<sup>4</sup>- and/or NR<sup>5</sup>R<sup>6</sup>- and/or alkyl, alkenyl and/or **[alkinyl]** **alkynyl** groups as substituents, wherein the residues R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> independently are defined as R<sup>1</sup> in claim 1, but are independent of R<sup>1</sup>, wherein

- (i) XY is excluded as group of formula -CH=CH- if R<sup>1</sup> is a hydrogen atom or a C<sub>1-4</sub>-alkyl group and R<sup>2</sup> is a monocyclic hetero aromatic having a N atom or a N and[/or] a S atom in its ring and a C<sub>1</sub>-alkyl substituent and
- (ii) XY is excluded as group of formula -CH<sub>2</sub>-CH-OP if R<sup>1</sup> is a hydrogen atom or a C<sub>1-4</sub>-alkyl group and R<sup>2</sup> is a monocyclic hetero aromatic having a N atom or a N and[/or] a S atom in its ring and a C<sub>1</sub>-alkyl substituent.

5. (Amended) [Epothilone derivative] A compound of the formula [(6)]:



wherein the residues are as defined in claim 4 and, if X-Y means a group of formula -CH<sub>2</sub>-CH-OP, the protective group P has been removed, wherein

- (i) XY is excluded as group of formula -CH=CH- if R<sup>1</sup> is a hydrogen atom or a C<sub>1-4</sub>-alkyl group and R<sup>2</sup> is a monocyclic hetero aromatic having a N atom and a S atom in its ring and a C<sub>1</sub>-alkyl substituent and
- (ii) XY is excluded as group of formula -CH<sub>2</sub>-CH-OP if R<sup>1</sup> is a hydrogen atom or a C<sub>1-4</sub>-alkyl group and R<sup>2</sup> is a monocyclic hetero aromatic having a N atom or a N atom and a S atom or a N atom and a O atom in its ring and a C<sub>1</sub>-alkyl substituent.

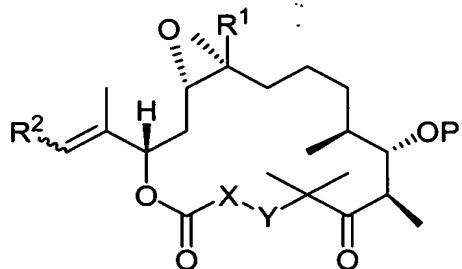
7. (Twice Amended) [Epothilone derivative] A compound as in claims 4, 5, 6 or 22 wherein the substituents of the monocyclic aromatic and/or hetero aromatic are C<sub>1-6</sub>-alkyl, C<sub>2-6</sub>-alkenyl and C<sub>2-6</sub>-[alkinyl] alkynyl groups respectively, and fluoro, chloro, bromo or iodo atoms.

8. (Amended) [Epothilone derivative] A compound as in claims 4, 5, 6, 7 or 22 wherein the monocyclic aromatic and monocyclic hetero aromatic, respectively, is provided with 1, 2 or 3 substituents and the hetero aromatic is provided with 1, 2 or more hetero atoms.

9. (Amended) Process for the production of a compound of [the formula (3)] claim 2, characterised in that a compound of [the formula (2)] claim 1 is reacted with a compound of the formula HC[B(OR)<sub>2</sub>]<sub>3</sub>, the radicals being as defined in one of the preceding claims and R being as defined for R<sup>1</sup> but being independent of R<sup>1</sup>.

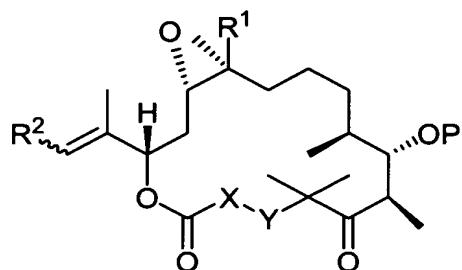
10. (Amended) Process for the production of a compound of [the formula (4)] claim 3, characterised in that a compound of [the formula (3)] claim 2 is reacted with N-iodo or N-bromo-succinimide and the radicals are as defined in one of the preceding claims.

11. (Amended) Process for the preparation of a compound of formula [(5),]:



wherein a compound [of formula (3)] according to claim 2 is reacted by a Suzuki coupling with a compound of formula  $R^2-Z$ , wherein  $R^2$  is a monocyclic aromatic which can be substituted by halogen atoms and/or  $OR^4$ - and/or  $NR^5R^6$ - and/or alkyl, alkenyl and/or [alkinyl] alkynyl groups in ortho and/or meta- and/or para-position, or a monocyclic 5- or 6-membered hetero aromatic, which can be provided with one or several O- and/or N- and/or S-atoms in the ring and/or which can be provided with  $OR^4$ - and/or  $NR^5R^6$ - and/or alkyl, alkenyl and/or [alkinyl] alkynyl groups as substituents and  $Z$  can be a halogen atom or a group of formula  $-OSO_2CF_3$ ,  $-CH=CHI$ ,  $-CH=CHSO_2CF_3$ .

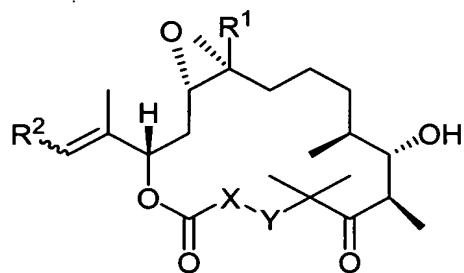
12. (Amended) Process for the preparation of a compound of formula [(5),]:



wherein a compound [of formula (4)] according to claim 3 is reacted by a silent coupling (stille Kupplung) with  $R_2-SNR^3_3$ , wherein  $R^2$  is a monocyclic aromatic which can be substituted by halogen atoms and/or  $OR^4$ - and/or  $NR^5R^6$ - and/or alkyl, alkenyl and/or

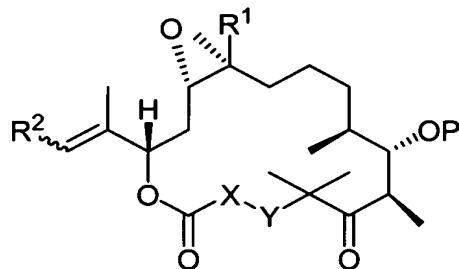
**[alkinyl] alkynyl** groups in ortho- and/or meta- and/or para-position, or a monocyclic 5- or 6-membered hetero aromatic, which can be provided with one or several O- and/or N- and/or S-atoms in the ring and/or which can be provided with  $OR^4$ - and/or  $NR^5R^6$ - and/or alkyl, alkenyl and/or **[alkinyl] alkynyl** groups as substituents and  $R^3$  is a  $C_{1-6}$ -alkyl group.

13. (Twice Amended) Process for the preparation of a compound of formula [(6),]:



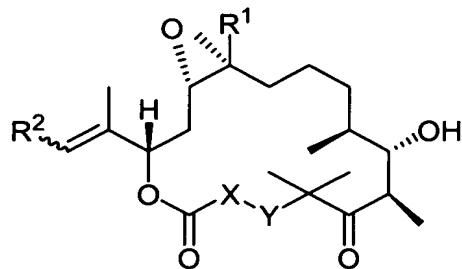
wherein the protective group is removed from a compound [of formula (5)] according to claim 4.

14. (Amended) Process for the preparation of a compound of formula [(6),]:



wherein it comprises the process steps as disclosed in claims 9, 10, 11, 12 or 13.

22. (Twice Amended) [Epothilone derivative] A compound of formula [(6),]:



wherein the residues are defined as in claim 4 and, if X-Y means a group of formula -  
CH<sub>2</sub>CH-OP, the protective group P has been removed, wherein

- (i) XY is excluded as group of formula -CH=CH- if R<sup>1</sup> is a hydrogen atom or a C<sub>1-4</sub>-alkyl group and R<sup>2</sup> is a monocyclic hetero aromatic having a N atom and/or a S atom in its ring and a C<sub>1</sub>-alkyl substituent and
- (ii) XY is excluded as group of formula -CH<sub>2</sub>-CH-OP if R<sup>1</sup> is a hydrogen atom or a C<sub>1-4</sub>-alkyl group and R<sup>2</sup> is a monocyclic hetero aromatic having a N atom or a N atom and[/or] a S atom or a N atom and[/or] an O atom in its ring and a C<sub>1</sub>- alkyl substituent.

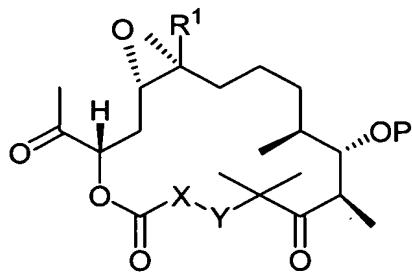
23. (Amended) **[Epothilone derivative]** A compound according to claim 22, wherein the substituents of the monocyclic aromatic and/or hetero aromatic are a C<sub>1-6</sub>-alkyl, C<sub>2-6</sub>-alkenyl **[and] or** C<sub>2-6</sub>-[alkinyl] alkynyl group[s respectively, especially C<sub>1-4</sub>-alkyl, C<sub>2-4</sub>-alkenyl and C<sub>2-4</sub>-akinyl groups, respectively and the] or a halogen atom[s fluoro, chloro, bromo or iodo atoms].

24. (Amended) **[Epothilone derivative]** A compound according to claim 22, wherein the monocyclic aromatic and monocyclic hetero aromatic, respectively, is provided with 1, 2 or 3 substituents and the hetero aromatic is provided with 1, 2 or more hetero atoms.

**EXHIBIT B**

**CLEAN VERSION OF THE PENDING CLAIM  
UPON ENTRY OF THE PRESENT AMENDMENT**

1. (Amended) A compound of the formula:



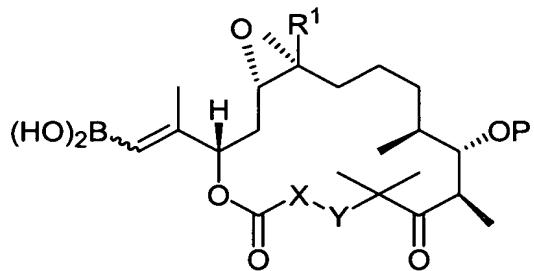
wherein

$R^1$  is a H atom or a  $C_1$ - to  $C_8$ -alkyl group,

$X-Y$  is a group of the formula  $-CH_2CH-OP$  or  $-CH=CH-$ , and

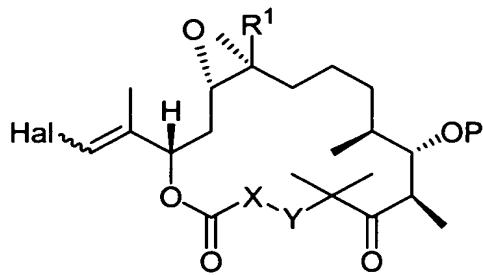
$P$  is a protecting group.

2. (Amended) A compound of the formula:



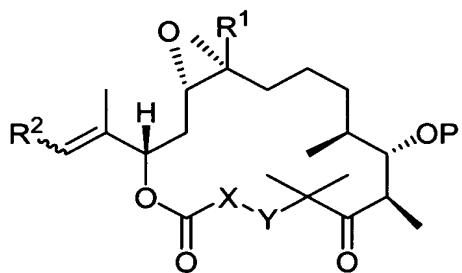
wherein the radicals are as defined in claim 1.

3. (Thrice Amended) A compound of formula:



wherein the residues R<sup>1</sup>, X-Y and P are defined as in claim 1, and Hal is a halogen.

4. (Twice Amended) A compound of the formula:

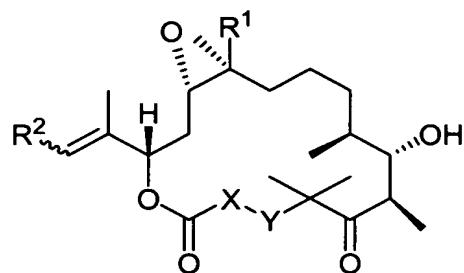


wherein the residue R<sup>1</sup> is a hydrogen atom or a C<sub>1-8</sub>-alkyl group, and P is a protective group and X-Y is a group of formula -CH<sub>2</sub>CH-OP or CH=CH, and R<sup>2</sup> is a monocyclic aromatic which can be substituted by a halogen atoms and/or OR<sup>4</sup>- and/or NR<sup>5</sup>R<sup>6</sup>- and/or alkyl, alkenyl and/or alkynyl groups in ortho- and/or meta- and/or para-position, or a monocyclic 5- or 6-membered hetero aromatic, which can be provided with one or several O- and/or N- and/or S-atoms in the ring and/or which can be provided with OR<sup>4</sup>- and/or NR<sup>5</sup>R<sup>6</sup>- and/or alkyl, alkenyl and/or alkynyl groups as substituents, wherein the residues R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> independently are defined as R<sup>1</sup> in claim 1, but are independent of R<sup>1</sup>, wherein

(i) XY is excluded as group of formula -CH=CH- if R<sup>1</sup> is a hydrogen atom or a C<sub>1-4</sub>-alkyl group and R<sup>2</sup> is a monocyclic hetero aromatic having a N atom or a N and a S atom in its ring and a C<sub>1</sub>-alkyl substituent and

(ii) XY is excluded as group of formula -CH<sub>2</sub>-CH-OP if R<sup>1</sup> is a hydrogen atom or a C<sub>1-4</sub>-alkyl group and R<sup>2</sup> is a monocyclic hetero aromatic having a N atom or a N and a S atom in its ring and a C<sub>1</sub>-alkyl substituent.

5. (Amended) A compound of the formula:



wherein the residues are as defined in claim 4 and, if X-Y means a group of formula -CH<sub>2</sub>-CH-OP, the protective group P has been removed, wherein

- (i) XY is excluded as group of formula -CH=CH- if R<sup>1</sup> is a hydrogen atom or a C<sub>1-4</sub>-alkyl group and R<sup>2</sup> is a monocyclic hetero aromatic having a N atom and a S atom in its ring and a C<sub>1</sub>-alkyl substituent and
- (ii) XY is excluded as group of formula -CH<sub>2</sub>-CH-OP if R<sup>1</sup> is a hydrogen atom or a C<sub>1-4</sub>-alkyl group and R<sup>2</sup> is a monocyclic hetero aromatic having a N atom or a N atom and a S atom or a N atom and a O atom in its ring and a C<sub>1</sub>-alkyl substituent.

6. (Amended) Epothilone derivative as in claims 1, 2, 3, 4, 5 or 22 wherein R<sup>1</sup>, R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> are a hydrogen atom or a C<sub>1-6</sub>-alkyl group.

7. (Twice Amended) A compound as in claims 4, 5, 6 or 22 wherein the substituents of the monocyclic aromatic and/or hetero aromatic are C<sub>1-6</sub>-alkyl, C<sub>2-6</sub>-alkenyl and C<sub>2-6</sub>-alkynyl groups respectively, and fluoro, chloro, bromo or iodo atoms.

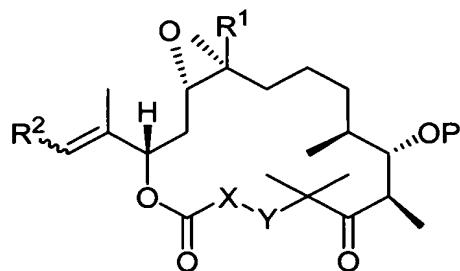
8. (Amended) A compound as in claims 4, 5, 6, 7 or 22 wherein the monocyclic aromatic and monocyclic hetero aromatic, respectively, is provided with 1, 2 or 3 substituents and the hetero aromatic is provided with 1, 2 or more hetero atoms.

9. (Amended) Process for the production of a compound of claim 2, characterised in that a compound of claim 1 is reacted with a compound of the formula HC[B(OR)<sub>2</sub>]<sub>3</sub>, the radicals

being as defined in one of the preceding claims and R being as defined for R<sup>1</sup> but being independent of R<sup>1</sup>.

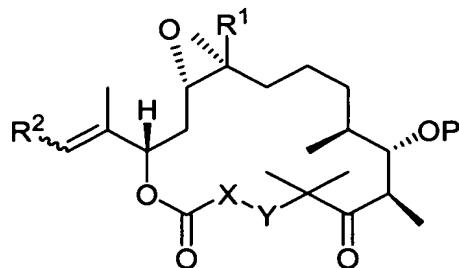
10. (Amended) Process for the production of a compound of claim 3, characterised in that a compound of claim 2 is reacted with N-iodo or N-bromo-succinimide and the radicals are as defined in one of the preceding claims.

11. (Amended) Process for the preparation of a compound of formula:



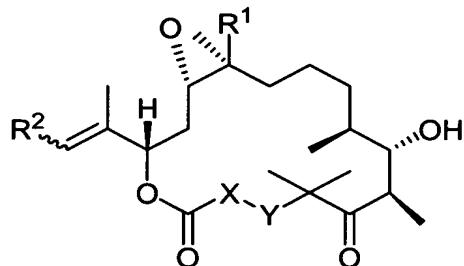
wherein a compound according to claim 2 is reacted by a Suzuki coupling with a compound of formula R<sup>2</sup>-Z, wherein R<sup>2</sup> is a monocyclic aromatic which can be substituted by halogen atoms and/or OR<sup>4</sup>- and/or NR<sup>5</sup>R<sup>6</sup>- and/or alkyl, alkenyl and/or alkynyl groups in ortho and/or meta- and/or para-position, or a monocyclic 5- or 6-membered hetero aromatic, which can be provided with one or several O- and/or N- and/or S-atoms in the ring and/or which can be provided with OR<sup>4</sup>- and/or NR<sup>5</sup>R<sup>6</sup>- and/or alkyl, alkenyl and/or alkynyl groups as substituents and Z can be a halogen atom or a group of formula -OSO<sub>2</sub>CF<sub>3</sub>, -CH=CHI, -CH=CHOSO<sub>2</sub>CF<sub>3</sub>.

12. (Amended) Process for the preparation of a compound of formula:



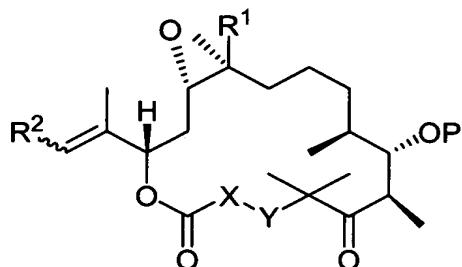
wherein a compound according to claim 3 is reacted by a silent coupling (stille Kupplung) with R<sub>2</sub>-SNR<sup>3</sup>, wherein R<sup>2</sup> is a monocyclic aromatic which can be substituted by halogen atoms and/or OR<sup>4</sup>- and/or NR<sup>5</sup>R<sup>6</sup>- and/or alkyl, alkenyl and/or alkynyl groups in ortho- and/or meta- and/or para-position, or a monocyclic 5- or 6-membered hetero aromatic, which can be provided with one or several O- and/or N- and/or S-atoms in the ring and/or which can be provided with OR<sup>4</sup>- and/or NR<sup>5</sup>R<sup>6</sup>- and/or alkyl, alkenyl and/or alkynyl groups as substituents and R<sup>3</sup> is a C<sub>1-6</sub>-alkyl group.

13. (Twice Amended) Process for the preparation of a compound of formula:



wherein the protective group is removed from a compound according to claim 4.

14. (Amended) Process for the preparation of a compound of formula:



wherein it comprises the process steps as disclosed in claims 9, 10, 11, 12 or 13.

15. (Canceled)

16. (Canceled)

17. (Canceled)

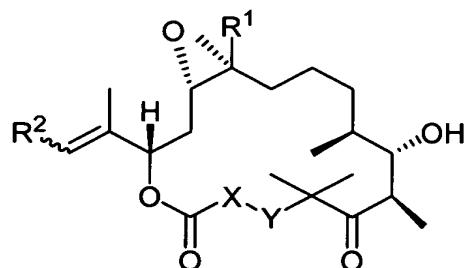
18. A pharmaceutical composition comprising at least one of the compounds described in claims 1, 2, 3, 4, 5, 6, 7, 8 or 22 and optionally carriers, diluents and/or auxiliary agents.

19. The pharmaceutical composition according to claim 18, wherein said compound is cytostaticum.

20. A method of protecting plants in agriculture and/or forest culture and/or horticulture, comprising administering a therapeutically effective amount of at least one compound described in claim 1 and optionally carriers, diluents and/or auxiliary agents.

21. (Cancelled)

22. (Twice Amended) A compound of formula:



wherein the residues are defined as in claim 4 and, if X-Y means a group of formula -CH<sub>2</sub>CH-OP, the protective group P has been removed, wherein

(i) XY is excluded as group of formula -CH=CH- if R<sup>1</sup> is a hydrogen atom or a C<sub>1-4</sub>-alkyl group and R<sup>2</sup> is a monocyclic hetero aromatic having a N atom and/or a S atom in its ring and a C<sub>1</sub>-alkyl substituent and

(ii) XY is excluded as group of formula -CH<sub>2</sub>-CH-OP if R<sup>1</sup> is a hydrogen atom or a C<sub>1-4</sub>-alkyl group and R<sup>2</sup> is a monocyclic hetero aromatic having a N atom or a N atom and a S atom or a N atom and an O atom in its ring and a C<sub>1</sub>-alkyl substituent.

23. (Amended) A compound according to claim 22, wherein the substituents of the monocyclic aromatic and/or hetero aromatic are a C<sub>1-6</sub>-alkyl, C<sub>2-6</sub>-alkenyl or C<sub>2-6</sub>-alkynyl group or a halogen atom.

24. (Amended) A compound according to claim 22, wherein the monocyclic aromatic and monocyclic hetero aromatic, respectively, is provided with 1, 2 or 3 substituents and the hetero aromatic is provided with 1, 2 or more hetero atoms.

25. (New) A compound according to claim 23, wherein the substituents of the monocyclic aromatic and/or hetero aromatic are C<sub>1-4</sub>-alkyl, C<sub>2-4</sub>-alkenyl and C<sub>2-4</sub>-alkynyl groups.